

Relationship Between Carotid Disease on Ultrasound and Coronary Disease on CT Angiography

Gerald I. Cohen, MD,* Rabeea Aboufakher, MD,† Renee Bess, RVT,* John Frank, MBBS,‡
Mahmoud Othman, MD,* Dennis Doan, MD,§ Nancy Mesiha, MD,*
Howard S. Rosman, MD,* Susan Szpunar, PhD*

Detroit, Michigan; Grand Forks, North Dakota; and Fort Worth, Texas

OBJECTIVES The purpose of this study was to assess the relationship between carotid artery disease by ultrasound and coronary artery disease by coronary computed tomography angiography (CTA) and to identify carotid ultrasound parameters predictive of coronary artery disease.

BACKGROUND Carotid ultrasound and CTA are noninvasive modalities used to image atherosclerosis. Studies examining the relationship between the 2 tests, however, are lacking.

METHODS We performed carotid ultrasound on predominantly nondiabetic subjects referred for CTA. Carotid intima media thickness (IMT) and plaque were assessed and compared with coronary artery calcification and the number of coronary arteries with any evidence of atherosclerosis on CTA.

RESULTS A total of 150 subjects underwent both CTA and carotid ultrasound on the same day. Carotid plaque was present in 71.3% (n = 107), whereas the presence of at least 1 coronary artery with disease on CTA was present in 57.1% (n = 84). Carotid plaque was present in 47.6% (30 of 63) of subjects with a calcium score of 0 and 88.5% (77 of 87) of subjects with a calcium score >0 (p = 0.0001). Similarly carotid plaque was present in 52.4% (33 of 63) of subjects with no CTA evidence of atherosclerosis versus 85.7% (72 of 84) of subjects with any CTA evidence of atherosclerosis (p < 0.0001). Carotid plaque, IMT ≥1.5 mm, or averaged mean IMT >0.75 mm were associated with a calcium score >0 (odds ratio: 5.4, p < 0.0001, 2.7, p < 0.001; 2.9, p = 0.011, respectively) and disease in at least 1 vessel on CTA (odds ratio: 2.8, p = 0.03, 2.19, p = 0.073; 2.22, p = 0.058, respectively) independent of age and sex.

CONCLUSIONS Carotid plaque and increased carotid IMT are associated with the presence and severity of coronary calcification and disease on CTA in ambulatory subjects. (J Am Coll Cardiol Img 2013;6:1160–7) © 2013 by the American College of Cardiology Foundation

From the *St. John Hospital and Medical Center, Detroit, Michigan; †Altru Health System, Grand Forks, North Dakota; ‡Henry Ford Hospital, Detroit, Michigan; and the §Heart Center of North Texas, Fort Worth, Texas. Dr. Othman is currently affiliated with the Detroit Medical Center, Detroit, Michigan. Supported by a grant from the Department of Graduate Medical Education at St. John Hospital and Medical Center, Detroit, Michigan. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received October 10, 2012; revised manuscript received May 31, 2013, accepted June 28, 2013.

Subclinical vascular disease may be detected in a number of ways, such as ultrasound of carotid intima media thickness (IMT) (1,2), computed tomography (CT) imaging of coronary artery calcium (CAC) (3), and, more recently, coronary computed tomography angiography (CTA) (4,5). Although carotid disease correlates with coronary artery disease (CAD) on invasive angiography (6,7) and CAC on CT (8), studies that compare carotid imaging and CTA are sparse, including 2 studies on diabetic or elderly Asian subjects (9,10). Our study further compares carotid IMT with coronary findings in predominantly nondiabetic, white patients undergoing 64-slice CTA for risk stratification. We hypothesize that carotid wall thickening and plaque are associated with coronary atherosclerosis on CTA and that the absence of carotid atherosclerosis predicts the absence of coronary disease.

See page 1168

METHODS

Study participants. Between September 2006 and June 2007, 150 consecutive ambulatory subjects underwent both CTA and carotid ultrasound on the same day. Subjects were mostly referred by their physicians for risk-stratification screening in 92 (61%), chest pain in 36 (24%), positive stress test in 14 (9%), dyspnea in 4 (3%), and follow-up of known CAD in 4 (3%). Patients paid for the scans out of pocket. Risk factors for CAD were identified by interviewing the patients before the CT scan and according to their current use of medications. Smoking status was defined as current, former, or never. Tests for fasting lipid profile and fasting blood glucose level were performed if no measurement had been performed in the previous 6 months. All subjects were recruited in a single institution and provided a written informed consent before enrollment. The St. John Hospital and Medical Center Institutional Review Board approved the study.

Coronary CTA. All patients received metoprolol succinate the evening before CTA and intravenous metoprolol or diltiazem during the examination as needed to achieve a heart rate of ≤ 60 beats/min. Sublingual nitroglycerin was administered. For the CTA datasets, a 64-slice system was used (GE LightSpeed VCT, Milwaukee, Wisconsin). Two volume datasets were collected: 1 noncontrast examination for calcium scoring and the other a

contrast-enhanced CTA examination for evaluating the coronary arteries. The calcified plaque burden was calculated from images acquired at a 2.5-mm slice collimation, tube energy of 120 kVp, tube current of 350 mA, and rotation speed of 500 ms. Retrospective gating with dose modulation was used. Images were reconstructed retrospectively, and the overall CAC score calculated according to the Agatston-Janowitz (AJ130) method from all calcified plaque in the coronary tree. For the contrast-enhanced CTA examination, a triphase injection protocol was used: the first phase consisting of 50 ml of Visipaque 320 (GE Healthcare, Cork, Ireland) followed by a second injection of a 2:3 mix of Visipaque 320 and saline solution, and a final phase of 35 ml of saline solution. Injection rate was 5 ml per second. The CTA volume datasets were acquired using retrospective electrocardiographic gating with a thinner slice collimation of 0.625 mm, a faster rotation speed of 350 ms, and a table pitch of 0.22. The tube energy remained at 120 kVp, but the current ranged from 400 to 700 mA, resulting in an estimated average effective radiation dose of 17 ± 6.6 mSv. The volumetric dataset was reconstructed at multiple phases (5) of the R-R interval using a 0.625-mm thickness and 0.4-mm spacing. The R-R interval for reconstruction was usually 60% to 80%, although this could vary if required for optimal imaging. Image quality was rated as adequate in 134 subjects and suboptimal in 16 subjects.

CT studies were reviewed (J.F.) for quantification of coronary atherosclerosis. The CAC score was categorized relative to cardiovascular disease (CVD) risk as 0 (0 Agatston score), mildly increased (1 to 99), moderately increased (100 to 399), and severely increased (≥ 400) (11). The number of coronary arteries with any evidence of atherosclerosis (calcified or noncalcified) regardless of degree of stenosis on CTA was counted to a maximum of 4 vessels: right coronary artery (including the posterior descending artery branch), circumflex coronary artery (including the first and second obtuse marginal branches), left anterior descending artery (including the first and second diagonal branches and ramus if present), and left main coronary artery. Similarly, the number of coronary arteries with $>50\%$ stenosis was counted (12).

Carotid ultrasound. Carotid imaging was performed with the subject supine using a linear array transducer (9L, GE Vivid 7, GE Ultrasound, Horten, Norway) with a fundamental frequency of 10 MHz. The transducer was placed above the clavicle, locating the

ABBREVIATIONS AND ACRONYMS

CAC	= coronary artery calcium
CAD	= coronary artery disease
CCA	= common carotid artery
CT	= computed tomography
CTA	= computed tomography angiography
CVD	= cardiovascular disease
ICA	= internal carotid artery
ICC	= intraclass correlation coefficient
IMT	= intima media thickness

common carotid artery (CCA), and then moved cephalad to the bifurcation, ending at the most distally visible internal carotid artery (ICA). Bilateral images were stored from digital capture of 3 cardiac cycles. Far wall mean IMT was measured offline at the electrocardiographic R-wave using GE EchoPAC automated border detection software of the following segments: the most distal 1 cm of the CCA before the bifurcation, the bifurcation segment between the CCA and the tip of the flow divider, and the most proximal 1-cm segment of the ICA (2). If image quality or surface irregularity prevented automated measurement, 10 measurements were made manually and averaged. A composite mean IMT was calculated by averaging the measured mean IMTs of the 6 segments.

Maximal IMT was the greatest near or far wall thickness, including plaque when present, that was manually measured at the electrocardiographic R-wave with the GE EchoPAC from the same segments imaged for the mean IMT. The presence of carotid plaque was based on ARIC (Atherosclerosis Risk In Communities) study criteria that required at least 2 of the following: an IMT >1.5 mm, change in the carotid wall surface contour, or focal change in the carotid wall echogenicity (13). Carotid measurements were obtained at the time of imaging (R.B.) and reviewed (G.I.C.) for measurement accuracy and the presence and location of plaque. Readers of the carotid and CT studies were blinded to patient demographics and clinical and alternate imaging data.

Statistical analysis. Descriptive data are presented as frequency and mean \pm SD. Chi-square analyses were used to examine associations between categorical variables. The Mantel-Haenszel chi-square test for linear trend was used to determine whether there was a linear trend in the percentage of individuals with carotid plaque by calcium score and number of coronary vessels with stenosis. Spearman's rho was used to examine correlations between continuous and categorical variables; Pearson correlation was used to examine linear associations between continuous variables. Means were compared using the Student *t* test or analysis of variance. Medians were compared using the Mann-Whitney *U* statistic. Logistic regression was used to model the probability of having a CAC score >0 or ≥ 1 diseased coronary vessels controlling for age, sex, and 2 categorical measures of IMT. Intraclass correlation coefficients (ICCs) were generated to determine interobserver and intraobserver variability for the maximal carotid IMT and CT calcium score. The kappa statistic was used to examine

interexaminer and intraexaminer variability in the number of coronary vessels with disease. All analyses were performed using IBM SPSS software, version 18.0 (New York, New York). A *p* value <0.05 was used to indicate statistical significance.

INTEREXAMINER AND INTRAEXAMINER VARIABILITY.

Inter-reader and intrareader variability of maximal IMT was determined. One reader (G.I.C.) reviewed 15 studies at 2 separate times and 2 readers (G.I.C. and R.B.) independently interpreted the same sample of images. Mean IMT variability, an automated measurement, was not obtained. The ICC for inter-rater agreement was 98% and the ICC for intrarater agreement was 99%. For CTA, 15 studies were reread by the original reader (J.F.) and independently read by a second reader (N.M.). For CAC score, the inter-observer and intraobserver variability had ICCs of 93% and 98%, respectively. For the number of coronary vessels with disease on CTA, the kappa statistics for interobserver and intraobserver variability were 72% and 91%, respectively.

RESULTS

Baseline characteristics. Table 1 lists participant characteristics, including 109 (73%) men 58.2 \pm 10.6 years of age. Subjects referred for screening were younger with less CAD on CT, hypertension, and diabetes compared with subjects with symptoms or known CAD. Otherwise, the 2 groups were not significantly different, including carotid IMT values. Risk factors for CAD were present in 130 (87%). A 10-year Framingham Risk Score for CVD events was low ($<6\%$ risk) in 31 (20.7%), intermediate (6% to 20% risk) in 70 (46.7%), and high ($>20\%$ risk) in 23 (15.3%) and not calculated in 26 (17.3%) because of known diabetes, CAD, or peripheral artery or renal disease (14).

Carotid ultrasound showed plaque in 107 (71%), including 13 (12%) with a maximal IMT of ≤ 1.5 mm. Quartile values for averaged mean IMT were ≤ 0.63 , 0.64 to 0.74, 0.75 to 0.85, and ≥ 0.86 mm. Quartile values for maximal IMT were ≤ 1.26 , 1.27 to 1.79, 1.80 to 2.69, and ≥ 2.7 mm. The maximal IMT was greatest for the far wall in 94 subjects and the near wall in 51 subjects, and the same for both walls in 5 subjects. Maximal IMT was measured at the bifurcation (1.4 ± 0.7 mm; range, 0.4 to 4.8 mm) in 109 subjects (73%), at the ICA (1.0 ± 0.6 mm; range, 0.3 to 4.4 mm) in 23 (15%), and at the CCA (1.0 ± 0.3 mm; range, 0.4 to 3.2 mm) in 18 (12%).

Atherosclerosis on CTA was not detectable at all in 63 subjects (43%) and could not be assessed in

3 subjects. Atherosclerosis involved 1 or 2 vessels in 46 (31%), 3 vessels in 25 (17%), and 4 vessels in 13 (9%) subjects. Occlusive disease >50% was present in 27.2% (40 of 147) subjects and involved 1 or 2 vessels in 34 (23.1%) subjects, 3 vessels in 3 (2%) subjects, and 4 vessels in 3 (2%) subjects.

The CAC score was 0 in 63 (42%), increased mildly in 35 (23%), moderately in 20 (13%), and severely in 32 (21%) subjects. Eight (9.5%) of 84 patients with any evidence of disease on CTA had a 0 calcium score.

Among 70 patients with an intermediate Framingham risk score, 48 (68.6%) had carotid plaque and 24 (34.2%) had at least intermediate CT findings, indicated by either a calcium score of ≥ 100 ($n = 21$) or evidence of either occlusive or at least 3-vessel atherosclerosis (an additional 3 subjects). Among the 48 with carotid plaque, 27 (56.2%) had lower risk CT findings and 21 (43.8%) had intermediate or worse CT findings. Among the remaining 22 subjects with no carotid plaque, 19 (86.4%) had a calcium score < 5 and 3 (13.6%) had at least intermediate CT findings, including 2 with occlusive disease and a calcium score of 330 and 747. Carotid plaque was present in 21 (87.5%) of 24 subjects with intermediate or worse CT findings and in 27 (58.7%) of 46 subjects with lower risk CT findings, including 7 (15.2%) with a maximal IMT in the highest quartile of > 2.7 mm.

Relationship between CAD and carotid artery disease. Subjects with CAD on CTA were older (62.1 ± 9.2 years of age with CAD vs. 53.0 ± 10.0 years of age with no CAD, $p < 0.0001$) and more likely to be male (66% of males vs. 33% of females with CAD, $p < 0.0001$). Similar findings were noted for patients with coronary calcification (61.7 ± 9.9 years of age with a CAC score > 0 vs. 53.3 ± 9.6 years of age with a CAC score of 0, $p < 0.0001$ and 67% of males vs. 34.1% of females with a CAC score > 0 , $p < 0.0001$). There was a significant correlation between CAC score and IMT (maximal and averaged mean IMT with $r = 0.30$, $p < 0.0001$ and $r = 0.21$, $p = 0.009$, respectively). Worsening carotid IMT was also associated with more coronary arteries with disease on CTA (Fig. 1).

Table 2 shows the maximal IMT, the averaged mean IMT, and the percentage of subjects with carotid plaque by CAC category and by the number of vessels with CAD on CTA. Carotid findings for patients with 1- and 2-vessel disease were similar, and so the data for these patients were merged. For the carotid plaque variable, the chi-square test for trend demonstrates a significant increasing trend in the percentage of subjects with carotid plaque with increasing CAC score ($p < 0.0001$). Similarly, there was a significant increase in the

Table 1. Baseline Characteristics of the Study Participants by Reason for Study

	Indication for Study		p Value
	Screening (n = 92)	Symptomatic (n = 58)	
Age, yrs	56.7 \pm 9.5	60.6 \pm 11.8	0.03
Body mass index, kg/m ²	28.4 \pm 4.8	29.5 \pm 5.2	0.19
Fasting glucose, mg/dl	93.4 \pm 18.2	97.9 \pm 30.4	0.32
Total cholesterol, mg/dl	195.0 \pm 41.9	182.7 \pm 39.5	0.08
Triglycerides, mg/dl	110.0 (74)	128.0 (97)	0.47
High-density lipoprotein, mg/dl	60.6 \pm 18.9	55.8 \pm 23.0	0.18
Low-density lipoprotein, mg/dl	106.9 \pm 38.3	99.9 \pm 34.5	0.27
Male	76.1	67.2	0.24
White	100	96.6	0.20
History of CAD	0.0	25.9	—
Diabetes	4.3	17.2	0.008
Hyperlipidemia	54.3	53.4	0.91
Hypertension	39.1	62.1	0.006
Family history of coronary disease	31.5	32.8	0.87
Chronic kidney disease	1.1	0.0	—
Peripheral vascular disease	1.1	0.0	—
Current smoker	6.5	5.2	0.74
Past smoker	39.1	31.0	0.31
Aspirin	54.3	67.2	0.12
Beta-blocker	19.6	43.1	0.002
ARB	10.9	13.8	0.59
ACE inhibitor	12.0	20.7	0.15
Statin	41.3	41.4	0.99
Diuretic	12.0	22.4	0.09
Maximal IMT, mm	2.1 \pm 0.96	2.0 \pm 1.0	0.70
Averaged IMT means, mm	0.77 \pm 0.17	0.81 \pm 0.21	0.23
Calcium score, Agatston score	232.4 \pm 556.2	475.8 \pm 984.2	0.09
Calcium score, Agatston score	20.5 (391)	5 (274)	0.34
No. of coronary arteries with disease	1.2 \pm 1.3	1.7 \pm 1.5	0.08
No. of coronary arteries with disease	1 (2)	2 (3)	0.05
No. of coronary arteries with >50% stenosis	0 (0)	0 (1)	0.19
No. of coronary arteries with >50% stenosis	0.34 \pm 0.71	0.67 \pm 1.1	0.04
CAC score of 0	42.4	41.4	0.9
Subjects with ≥ 1 more vessels with >50% stenosis	23.6	32.8	0.22

Values are mean \pm SD, %, or median (interquartile range).
 ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; CAC = coronary artery calcium; CAD = coronary artery disease; IMT = intima media thickness.

percentage of subjects with carotid plaque as the number of vessels with CAD on CTA increased (chi-square test for trend, $p < 0.0001$).

After examining the data, we chose a cut point of 0.75 for the average mean IMT and 1.5, a criteria

Table 2. Differences in Carotid IMT and Presence of Plaque by Categorical Coronary Artery Calcium Score and Number of Coronary Arteries With Any Evidence of Atherosclerosis on CT

	Coronary Artery Calcium (Agatston Score)				Test Statistic	p Value
	0	1-99	100-399	400+		
Maximal carotid IMT	1.61 ± 0.78	2.08 ± 0.88	2.48 ± 0.91*	2.64 ± 1.06†	F = 11.5	<0.0001
Mean of 6 segment IMT means	0.71 ± 0.18	0.79 ± 0.21	0.84 ± 0.17‡	0.87 ± 0.15§	F = 6.4	<0.0001
Plaque present	47.6% (30/63)	85.7% (30/35)	90.0% (18/20)	90.6% (29/32)	$\chi^2_{\text{trend}} = 21.8$	<0.0001

	No. of Coronary Arteries With Any Disease				Statistic	p Value
	0	1-2	3	4		
Maximal carotid IMT	1.62 ± 0.74	2.18 ± 0.92	2.41 ± 0.95	2.98 ± 1.13¶#	F = 11.6	<0.0001
Mean of 6 segment IMT means	0.72 ± 0.18	0.80 ± 0.19	0.86 ± 0.17**	0.90 ± 0.14††	F = 6.4	<0.0001
Plaque present	52.4 (33/63)	82.6 (38/46)	88.0 (22/25)	92.3 (12/13)	$\chi^2_{\text{trend}} = 17.1$	<0.0001

Values are mean ± SD or % (n/N). Multiple pairwise comparisons were computed using the Bonferroni correction: *Maximal carotid IMT in individuals with a CAC score of 100 to 399 versus a CAC score of 0 (p = 0.001). †Maximal carotid IMT with a CAC score of ≥400 versus a CAC score of 0 (p < 0.0001). ‡Mean of all 6 segment IMT with a CAC score of 100 to 399 versus a CAC score of 0 (p = 0.05). §Mean of all 6 segment IMT with a CAC of ≥400 versus a CAC score of 0 (p < 0.0001). ||Maximal carotid IMT with 3 diseased vessels versus 0 diseased vessels (p = 0.001). ¶Maximal carotid IMT with ≥4 diseased vessels compared with those with 0 diseased vessels (p < 0.0001). #Maximal carotid IMT with ≥4 diseased vessels compared with those with 1 or 2 diseased vessels (p = 0.025). **Mean of all 6 segment IMT means with 3 diseased vessels versus 0 diseased vessels (p = 0.004). ††Mean of all 6 segment IMT means with ≥4 diseased vessels versus 0 diseased vessels (p = 0.007). CAC = coronary artery calcium; CT = computed tomography; IMT = intima media thickness.

for plaque, for the maximal IMT. Logistic regression was then used to model the probability of having a CAC score >0 or at least 1 diseased coronary vessel after controlling for age, sex, and either the categorical mean IMT or categorical maximal IMT score. As seen in Table 3, both the maximal and averaged mean IMT measures and the presence of carotid plaque predicted an increased probability of coronary disease, after controlling for age and sex.

Carotid plaque was present in 47.6% (30 of 63) of subjects with a CAC score of 0 and 88.5% (77 of 87) of subjects with a CAC score >0 (p = 0.0001). Similarly, carotid plaque was present in 52.4% (33 of 63) of subjects with no CTA evidence of atherosclerosis versus 85.7% (72 of 84) of subjects with any CTA evidence of atherosclerosis (p < 0.0001). A maximal carotid IMT of ≥1.5 mm or the presence of carotid plaque was similarly predictive of CAD with a positive predictive value of 70% and 69%, respectively, for disease involving at least 1 vessel on CTA (compared with 71% and 72% for a CAC score >0). The negative predictive value of IMT <1.5 mm or no carotid plaque for CAD was 67% and 71%, respectively, for no disease affecting any vessel on CTA (vs. for 67% and 77%, respectively, for a CAC score of 0). An averaged mean IMT of at least 0.75 mm or maximal IMT of at least 1.5 mm similarly distinguished patients with CAD by CAC score or by at least 1 vessel with disease on CTA. However, disease predictability and reassurance were imperfect; a given patient could have severe disease at 1 arterial site and little or no disease at the other.

DISCUSSION

The relationship between carotid and coronary artery atherosclerosis. Our study demonstrated that carotid plaque and increased IMT are associated with CAD on CTA in a mostly nondiabetic white cohort. Our findings were consistent with those of previous studies that found an association between carotid artery disease and CAD by invasive coronary angiography (6,7) and CAC on CT (15,16). We compared carotid IMT measurements with the numbers of coronary arteries with any amount of disease and found a significant and similar relationship irrespective of how carotid artery disease and CAD was measured or defined (by maximal or mean IMT, the presence of carotid plaque, CAC score, and number of diseased arteries on CTA). We found modest correlations, comparable to other studies, between IMT and CAC, but greater for maximal than mean IMT. Like Lim *et al.* (9), we found that coronary atherosclerosis on CAC and CTA were similarly related to carotid disease. Carotid plaque, maximal IMT ≥1.5 mm and averaged mean IMT >0.75 mm predicted CAD independent of age and sex. Plaque had a closer relationship with CAD than maximal or average mean IMT, especially to CAC. CAD was present in most patients with carotid plaque or increased IMT (maximal IMT ≥1.5 mm or mean IMT >0.75 mm) and absent in most patients without carotid plaque or with lower IMT values.

Our findings are similar to those of Sillesen *et al.* (1) who examined subclinical atherosclerosis in an older population and found a stronger relationship between CAC and 3-dimensional carotid plaque

burden than mean CCA IMT. They similarly found carotid plaque in more subjects (78% vs. our 71%) than a non-0 calcium score (68% vs. our 58%).

The relationship that we found between carotid IMT and CAD on CT supports the concept that atherosclerosis is a systemic process. However, modest correlations indicate that atherosclerosis may have a heterogeneous distribution. This relationship may be affected by risk factor profile. Bauer *et al.* (17) found that carotid IMT was more closely related to diabetes, and CAC was more closely related to hypertension. Subclinical aortic, coronary, and carotid atherosclerosis had low correlations in the Framingham offspring study (18). The possibility that atheroma is detectable at just 1 site, therefore, may recommend multisite or multi-modality imaging to avoid false reassurance.

Methodological considerations. We compared how measuring carotid and coronary disease in different ways affects the association of disease between these 2 sites. For example, we compared measurement of maximal and averaged mean IMT. Mean IMT takes more time when automated measurement is not possible because of suboptimal images or plaque irregularity or calcification. In our experience, maximal IMT, although not a standard parameter, is practical in identifying the presence of plaque for rapid risk assessment. Most (>90%) of our patients with the adverse finding of carotid plaque had an IMT ≥ 1.5 mm (13). Furthermore, maximal IMT was not inferior to averaged mean IMT in its correlation with CAD and similarly related to calcium score and the number of coronary arteries with any degree of CAD. On the other hand, simply counting the number of coronary arteries with any evidence of atherosclerosis on CT might seem to be a simplified way of quantifying CAD compared with more precise segment-by-segment quantification of coronary plaque burden, but it was not inferior to calcium score, which missed some patients with noncalcified CAD (19,20). In addition, the criteria of any evidence of atherosclerosis represented a low threshold for the detection of CAD.

The MESA (Multi-Ethnic Study of Atherosclerosis) found coronary calcium was a greater predictor of CVD than carotid IMT (21), indicating a closer clinical connection when imaging is performed at the same site of disease. Although recent studies suggest little or no incremental value of using carotid IMT for assessing CAD risk (22,23), the disadvantages of CT should inspire re-evaluation of preferred carotid IMT methodology. Disadvantages of CT include radiation, cost, portability, disease monitoring, and diagnostic and

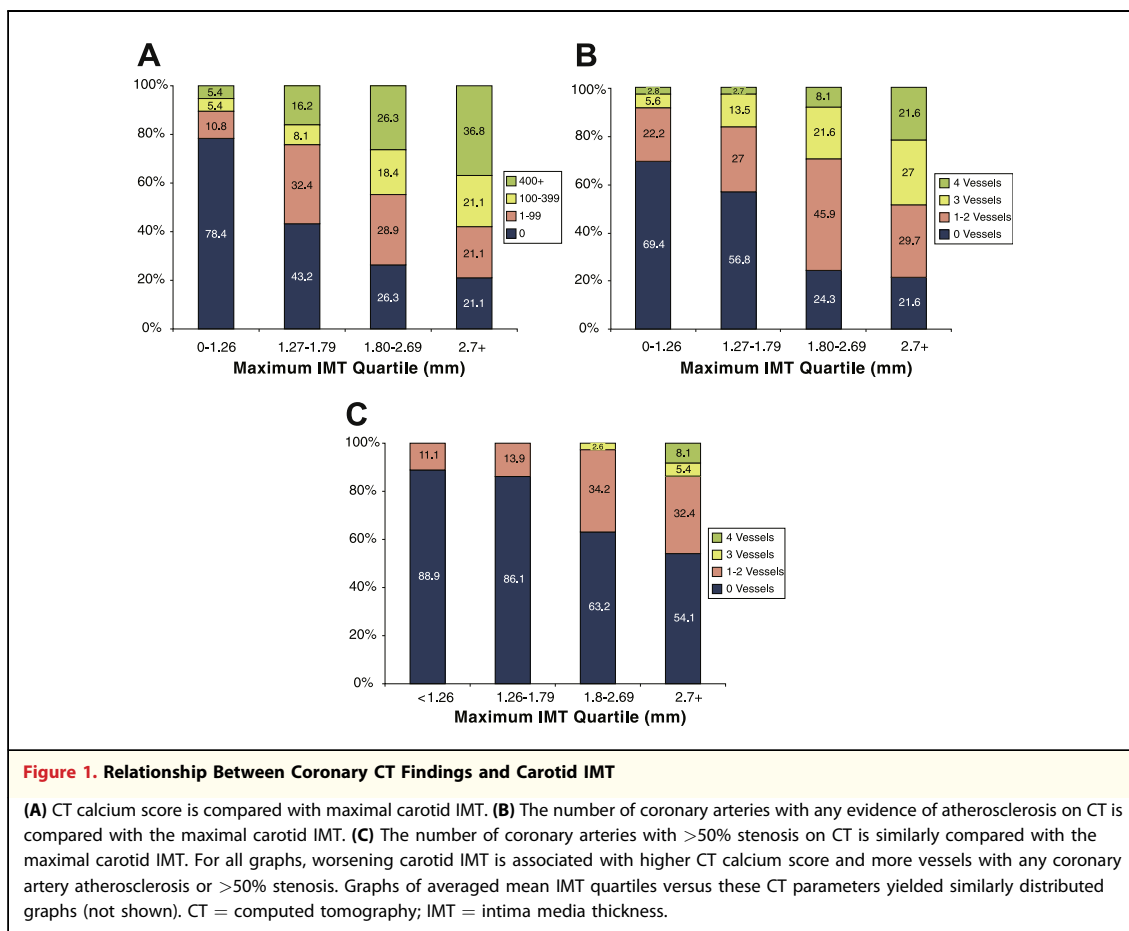
Table 3. Multivariate Analysis, IMT Measurement, and the Probability of a CAC Score >0 or at Least 1 Coronary Artery With Any Evidence of Atherosclerosis on CT After Controlling for Age and Sex

	Odds Ratio	p Value	95% CI
Model 1: predicting CAC > 0			
Age	1.09	0.001	1.04–1.14
Male	4.69	0.001	1.89–11.61
Avg. of 6 segment mean IMT >0.75	2.86	0.011	1.26–6.44
Model 2: predicting ≥ 1 diseased coronary vessels			
Age	1.11	<0.0001	1.05–1.16
Male	5.09	0.001	1.98–13.06
Avg. of 6 segment mean IMT >0.75	2.22	0.058	0.98–5.07
Model 3: predicting CAC >0			
Age	1.09	<0.001	1.04–1.14
Male	5.26	<0.001	2.14–12.96
Max IMT ≥ 1.5	2.71	<0.001	1.17–6.28
Model 4: predicting ≥ 1 diseased coronary vessels			
Age	1.11	<0.0001	1.06–1.17
Male	5.58	<0.0001	2.19–14.26
Max IMT ≥ 1.5	2.19	0.073	0.93–5.16
Model 5: Predicting CAC >0			
Age	1.08	0.002	1.03–1.13
Male	5.92	<0.0001	2.34–14.95
Plaque present	5.38	<0.0001	2.1–13.81
Model 6: predicting ≥ 1 diseased coronary vessels			
Age	1.11	<0.0001	1.05–1.16
Male	5.93	<0.0001	2.31–15.2
Plaque present	2.81	0.03	1.11–7.10

CI = confidence interval; other abbreviations as in Tables 1 and 2.

subsequent therapeutic error impact (19,24,25). Carotid imaging has complementary advantages and may be especially useful when applied in younger or higher risk patients with lucent plaque and negative CT findings (26,27). A study by Polak *et al.* (28) noted detection of carotid plaque and measurement of maximal internal carotid IMT was superior in predicting CVD risk than mean common carotid IMT assessment. In our study, atherosclerosis was more prevalent by carotid ultrasound, especially at the bifurcation, than on coronary CT.

Study limitations. The U.S. Preventive Services Task Force has not endorsed carotid IMT or



CT calcium scoring for screening subclinical atherosclerosis (29). However, statements by the American College of Cardiology/American Heart Association and American Society of Echocardiography (2) support using these modalities to refine risk stratification and management of patients at intermediate risk (3,13,30). The long-term and incremental impact of screening on outcome needs to be established further (18). Preferred screening modalities may need to be selected differently to specific populations. The application of our findings may be limited by the nature of our study population, which was mostly white men with a significant minority of non-screening examinations.

CONCLUSIONS

Carotid IMT and plaque are associated with the presence and degree of coronary calcification and disease on CTA. Because correlations between modalities are modest, the selection of an imaging modality should be guided by patient and methodological considerations and recognition of the heterogeneous distribution of atherosclerosis.

Reprint requests and correspondence: Dr. Gerald I. Cohen, St. John Hospital and Medical Center, Non-Invasive Cardiology, 22101 Moross Road, Suite 1N031, Detroit, Michigan 48236. *E-mail:* gerald.cohen@stjohn.org.

REFERENCES

- Sillescu H, Muntendam P, Adourian A, et al. Carotid plaque burden as a measure of subclinical atherosclerosis: comparison with other tests for subclinical arterial disease in the High Risk Plaque BioImage study. *J Am Coll Cardiol Img* 2012;5:681-9.
- Stein JH, Korcarz CE, Hurst RT, et al. Use of carotid ultrasound to identify subclinical vascular disease and evaluate cardiovascular disease risk: a consensus statement from the American Society of Echocardiography Carotid Intima-Media Thickness Task

- Force. Endorsed by the Society for Vascular Medicine. *J Am Soc Echocardiogr* 2008;21:93-111.
3. Greenland P, Bonow RO, Brundage BH, et al. ACCF/AHA 2007 clinical expert consensus document on coronary artery calcium scoring by computed tomography in global cardiovascular risk assessment and in evaluation of patients with chest pain: a report of the American College of Cardiology Foundation Clinical Expert Consensus Task Force (ACCF/AHA Writing Committee to Update the 2000 Expert Consensus Document on Electron Beam Computed Tomography). *J Am Coll Cardiol* 2007;49:378-402.
4. Ropers D, Baum U, Pohle K, et al. Detection of coronary artery stenoses with thin-slice multi-detector row spiral computed tomography and multiplanar reconstruction. *Circulation* 2003;107:664-6.
5. Achenbach S, Moselewski F, Ropers D, et al. Detection of calcified and non-calcified coronary atherosclerotic plaque by contrast-enhanced, submillimeter multidetector spiral computed tomography: a segment-based comparison with intravascular ultrasound. *Circulation* 2004;109:14-7.
6. Craven TE, Ryu JE, Espeland MA, et al. Evaluation of the associations between carotid artery atherosclerosis and coronary artery stenosis. A case-control study. *Circulation* 1990;82:1230-42.
7. Akosah KO, McHugh VL, Barnhart SI, et al. Carotid ultrasound for risk clarification in young to middle-aged adults undergoing elective coronary angiography. *Am J Hypertens* 2006;19:1256-61.
8. Arad Y, Spadaro LA, Roth M, et al. Correlations between vascular calcification and atherosclerosis: a comparative electron beam CT study of the coronary and carotid arteries. *J Comput Assist Tomogr* 1998;22:207-11.
9. Lim S, Choi HJ, Shin H, et al. Subclinical atherosclerosis in a community-based elderly cohort: the Korean Longitudinal Study on Health and Aging. *Int J Cardiol* 2012;155:126-33.
10. Djaber R, Schuijff JD, de Koning EJ, et al. Usefulness of carotid intima-media thickness in patients with diabetes mellitus as a predictor of coronary artery disease. *Am J Cardiol* 2009;104:1041-6.
11. Berman DS, Wong ND, Gransar H, et al. Relationship between stress-induced myocardial ischemia and atherosclerosis measured by coronary calcium tomography. *J Am Coll Cardiol* 2004;44:923-30.
12. Raff GL, Abidov A, Achenbach S, et al. SCCT guidelines for the interpretation and reporting of coronary computed tomographic angiography. *J Cardiovasc Comput Tomogr* 2009;3:122-36.
13. Nambi V, Chambless L, Folsom AR, et al. Carotid intima-media thickness and presence or absence of plaque improves prediction of coronary heart disease risk: the ARIC (Atherosclerosis Risk In Communities) study. *J Am Coll Cardiol* 2010;55:1600-7.
14. D'Agostino RB Sr., Vasan RS, Pencina MJ, et al. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. *Circulation* 2008;117:743-53.
15. Davis PH, Dawson JD, Mahoney LT, Lauer RM. Increased carotid intimal-media thickness and coronary calcification are related in young and middle-aged adults. The Muscatine study. *Circulation* 1999;100:838-42.
16. Oei HH, Vliegenthart R, Hak AE, et al. The association between coronary calcification assessed by electron beam computed tomography and measures of extracoronary atherosclerosis: the Rotterdam Coronary Calcification Study. *J Am Coll Cardiol* 2002;39:1745-51.
17. Bauer M, Mohlenkamp S, Lehmann N, et al. The effect of age and risk factors on coronary and carotid artery atherosclerotic burden in males-Results of the Heinz Nixdorf Recall Study. *Atherosclerosis* 2009;205:595-602.
18. Kathiresan S, Larson MG, Keyes MJ, et al. Assessment by cardiovascular magnetic resonance, electron beam computed tomography, and carotid ultrasonography of the distribution of subclinical atherosclerosis across Framingham risk strata. *Am J Cardiol* 2007;99:310-4.
19. Rosen BD, Fernandes V, McClelland RL, et al. Relationship between baseline coronary calcium score and demonstration of coronary artery stenoses during follow-up MESA (Multi-Ethnic Study of Atherosclerosis). *J Am Coll Cardiol Img* 2009;2:1175-83.
20. Steinvil A, Sadeh B, Arbel Y, et al. Prevalence and predictors of concomitant carotid and coronary artery atherosclerotic disease. *J Am Coll Cardiol* 2011;57:779-83.
21. Folsom AR, Kronmal RA, Detrano RC, et al. Coronary artery calcification compared with carotid intima-media thickness in the prediction of cardiovascular disease incidence: the Multi-Ethnic Study of Atherosclerosis (MESA). *Arch Intern Med* 2008;168:1333-9.
22. Den Ruijter HM, Peters SA, Anderson TJ, et al. Common carotid intima-media thickness measurements in cardiovascular risk prediction: a meta-analysis. *JAMA* 2012;308:796-803.
23. Yeboah J, McClelland RL, Polonsky TS, et al. Comparison of novel risk markers for improvement in cardiovascular risk assessment in intermediate-risk individuals. *JAMA* 2012;308:788-95.
24. Henneman MM, Schuijff JD, Pundziute G, et al. Noninvasive evaluation with multislice computed tomography in suspected acute coronary syndrome: plaque morphology on multislice computed tomography versus coronary calcium score. *J Am Coll Cardiol* 2008;52:216-22.
25. Nissen SE. Coronary computed tomography angiography. The challenge of coronary calcium. *J Am Coll Cardiol* 2012;59:388-9.
26. Honda O, Sugiyama S, Kugiyama K, et al. Echolucent carotid plaques predict future coronary events in patients with coronary artery disease. *J Am Coll Cardiol* 2004;43:1177-84.
27. Lester SJ, Eleid MF, Khandheria BK, Hurst RT. Carotid intima-media thickness and coronary artery calcium score as indications of subclinical atherosclerosis. *Mayo Clin Proc* 2009;84:229-33.
28. Polak JF, Pencina MJ, Pencina KM, O'Donnell CJ, Wolf PA, D'Agostino RB Sr. Carotid-wall intima-media thickness and cardiovascular events. *N Engl J Med* 2011;365:213-21.
29. U.S. Preventive Services Task Force. Using nontraditional risk factors in coronary heart disease risk assessment: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 2009;151:474-82.
30. Rozanski A, Gransar H, Shaw LJ, et al. Impact of coronary artery calcium scanning on coronary risk factors and downstream testing the EISNER (Early Identification of Subclinical Atherosclerosis by Noninvasive Imaging Research) prospective randomized trial. *J Am Coll Cardiol* 2011;57:1622-32.

Key Words: atherosclerosis ■ carotid ultrasound ■ coronary CT angiography.